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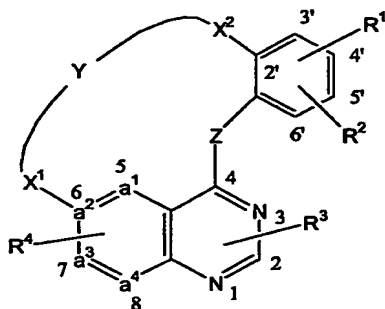
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(54) Title: PYRIDO- AND PYRIMIDOPYRIMIDINE DERIVATIVES AS ANTI-PROLIFERATIVE AGENTS



(57) Abstract: The present invention concerns the compounds of formula (I) the *N*-oxide forms, the pharmaceutically acceptable addition salts and the stereochemically isomeric forms thereof, wherein  $a^1-a^2=a^3-a^4$  represents a divalent radical selected from  $N-CH=CH-CH$ ,  $N-CH-N-CH$  or  $CH-CH=N-CH$ ; Z represents NH; Y represents  $-C_{3-9}alkyl-$ ,  $-C_{1-5}alkyl-NR^{13}-C_{1-5}alkyl-$ ,  $-C_{1-6}alkyl-NH-CO-$  or  $-CO-NH-C_{1-6}alkyl-$ ;  $X^1$  represents  $-O-$  or  $-NR^{11}-$ ;  $X^2$  represents  $-C_{1-2}alkyl-$ ,  $-O-C_{1-2}alkyl-$ ,  $-O-$  or  $-O-CH_2-$ ;  $R^1$  represents hydrogen or halo;  $R^2$  represents hydrogen, cyano, halo, hydroxycarbonyl- $C_{1-4}alkyloxy$ carbonyl-,  $Het^{16}$ -carbonyl- or  $Ar^5$ ;  $R^3$  represents hydrogen;  $R^4$  represents hydroxy,  $C_{1-4}alkyloxy-$ ,  $Ar^4-C_{1-4}alkyloxy$  or  $R^4$  represents  $C_{1-4}alkyloxy$  substituted with one or where possible two or more substituents selected from  $C_{1-4}alkyloxy-$  or  $Het^2$ ;  $R^{11}$  represents hydrogen;  $R^{12}$  represents hydrogen,  $C_{1-4}alkyl-$  or  $C_{1-4}alkyl-oxy$ -carbonyl-;

$R^{13}$  represents  $Het^{14}-C_{1-4}alkyl$ , in particular morpholinyl- $C_{1-4}alkyl$ ;  $Het^2$  represents a heterocycle selected from morpholinyl or piperidinyl optionally substituted with  $C_{1-4}alkyl$ -, preferably methyl;  $Het^{14}$  represents morpholinyl;  $Het^{16}$  represents a heterocycle selected from morpholinyl or pyrrolidinyl;  $Ar^4$  represents phenyl;  $Ar^5$  represents phenyl optionally substituted with cyano.



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- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations
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